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## Association between transportation noise and cardio-metabolic diseases: an update of the WHO meta-analysis

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### ABSTRACT

For the development of the WHO Noise Guidelines for the European Region, meta-analyses for various cardio-metabolic outcomes were conducted to derive exposure-response associations for road traffic, aircraft and railway noise. Papers published until 2015 were considered. Since then, several new studies have been published. In the framework of revision of regulatory noise limits in Switzerland, up to date evidence for the health effects of noise is needed. Thus, the aim was to update recent meta-analyses for incidence of ischemic heart disease (IHD) and diabetes with studies published until February 2019. The same protocol was applied as done by the WHO Environmental Noise Guideline group. Systematic literature search followed the search strategy of the WHO. Risk of bias for each study was evaluated for various design aspects. Pooled exposure-response associations were calculated for road traffic, aircraft and railway noise based on fixed or random-effects model depending on the outcome of the Cochran's Q-test and the I<sup>2</sup>-statistic, which reflects the percentage of between-study heterogeneity. Thirteen studies were included in the IHD meta-analysis, contributing 13 risk estimates for road traffic, 5 for aircraft and 3 for railway noise exposure. Only the result for road traffic noise reached statistical significance (1.02 [1.00 – 1.04] per 10 dB Lden). For diabetes, 6 studies were included, contributing 5 risk estimates for road traffic, 3 for aircraft and 2 for railway noise exposure. Again, only the road traffic noise result was statistically significant (1.11 [1.08 – 1.15] per 10 dB Lden). Here we present the updated evidence and exposure-response analysis for Lden, and discuss whether and how evidence for ischemic heart disease and diabetes has changed in the last few years.

Keywords: Source-specific noise, Incidence, Guideline limits

### 1. INTRODUCTION

Transportation noise, especially in our built-up areas and cities, is a part of daily life and an important risk factor for chronic disease. Epidemiological literature aimed to elucidate associations between transportation noise and adverse cardio-metabolic health effects is steadily increasing (1-5). Recently a comprehensive review has been conducted to develop the WHO Environmental Noise Guidelines for the European Region (6, 7). It included studies published between January 2000 and August 2015. While guideline values were largely set on the basis of the annoyance findings, it also reported an increased relative risks (RR) for ischemic heart disease (IHD) incidence and both road traffic noise (1.08 [95% confidence interval (CI): 1.01–1.15] per 10 dB Lden) and aircraft noise (1.09 [1.04 – 1.15] per 10 dB Lden). No studies on railway noise and IHD incidence were available. Few studies also reported associations between transportation noise and IHD mortality or diabetes. Since the cut-off date for inclusion in the Environmental Noise Guidelines, several new studies have been published.

Switzerland is currently undertaking a revision of its regulatory noise limits. To do so, the approach of the WHO noise guidelines was used in a slightly adapted manner: First, key outcomes with sufficient evidence for noise effects, and with sufficient survey or epidemiological data to derive exposure-response functions, were selected. This included noise annoyance, sleep disturbances, ischemic heart diseases and diabetes. Second, for each of these outcomes, acceptable risk attributable to noise exposure was determined taking into account their disability weights. Third, exposure-response functions for each outcome were obtained or derived for road, railway and aircraft

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noise to determine the noise level with acceptable risk. To this end, we aimed to review and update relevant sections of the WHO guidelines to incorporate new studies on incidence of IHD and diabetes published until February 2019 to derive updated exposure-response functions.

## 2. METHOD

For the systematic review and meta-analysis, the same protocol used by the WHO Environmental Noise Guideline group was followed. This included: applying the same search strategy (see section 2.1) and evaluating the risk of bias (RoB) for all exposure-outcome pairs in each study (adapted from (8)). Pooled exposure-response associations were calculated separately for road, railway and aircraft noise using fixed or random-effects meta-analysis depending on the outcome of the Cochran's Q-test and the I<sup>2</sup>-statistic, and presented graphically in Forest plots.

For incidence of IHD, the meta-analyses presented in Figures 1 (road traffic noise) and 10 (aircraft noise) in the Environmental Noise Guidelines were updated (6). A more recent systematic review and meta-analysis was used as the starting point for updating the meta-analysis on diabetes incidence (9). These are subsequently referred to as the "start meta-analyses (start MA)."

### 2.1 Literature search and selection criteria

The literature search was conducted for the period 01.01.2014 to 01.03.2019. The OVID search from van Kempen (7) was slightly modified to exclude outcomes not of interest at the outset. A PubMed search was also included for IHD following that used in our previous publication by Vienneau (10). The search strings are presented in Annex 1. The search was supplemented with recent publications maintained in the author's collections, identified previously through hand searching and/or email alerts.

The following inclusion/exclusion criteria were applied:

- a) Studies on road traffic, railway or aircraft noise exposure and incidence of IHD or diabetes (excluding gestational diabetes) were retained; those only reporting prevalence and/or mortality were excluded.
- b) Accepted study designs were cohorts, case-control and small-area studies.
- c) Exposure had to be modelled or measured. Eligible studies had to quantify the association in dB by a linear trend or in categories from which the linear trend could be calculated. RRs were expressed per 10 dB Lden prior to pooling (10).
- d) Studies were only included if basic adjustment for socio-economic status was performed.

For eligible studies, risk estimates were extracted using the following selection criteria:

- e) For IHD, studies that were exclusively non-fatal or combined fatal and non-fatal incident myocardial infarction (MI) or IHD were accepted. If both MI and IHD were available, risk estimates for IHD were selected.
- f) Modelled community noise was included only for the predominant source (e.g., if road traffic noise was the main source, risk estimates for community noise exposure were included in the road traffic noise meta-analysis).
- g) If available, the risk estimates adjusted for air pollution were selected. When several models were presented in a single study, the NO<sub>x</sub>-adjusted risk estimate was selected over the PM-adjusted on the basis of NO<sub>2</sub> being the better proxy for traffic related air pollution.
- h) Retained studies were cross-checked against those previously included in each start MA to ensure no duplication of study populations. Where relevant, the most recent results (i.e. with larger population or longer follow-up) were retained.

## 3. RESULTS

### 3.1 Study and risk estimate selection

The OVID search returned 31 and 55 hits for IHD and diabetes, respectively and the PubMed search for IHD returned 81 hits. The study selection process is outlined in Figure 1. After removing duplicates, studies already in the start MA, abstract screening and application of the selection criteria during full-text evaluation, a total of 7 and 3 new studies were respectively retained for IHD (11-17) and

diabetes (13, 18, 19). Studies in the start MA were reintroduced at the end of the study selection process, after verification that the inclusion/exclusion and selection criteria were still met.

Two recent studies were included through scanning the author’s collections, specifically Pyko (15) and Ohlwein (18). Two studies did not meet the inclusion criteria and were excluded during full text evaluation: de Kluizenaar (20) because the reported RR was for IHD and cerebrovascular disease combined, and the Kaunas study by Grazuleviciene (21) because it did not have any adjustment for SES. Finally, three replacement studies were identified: for IHD, Sørensen (22) was replaced by Roswall (16) with longer follow up; for diabetes, Sørensen (23) was replaced by Roswall (19) with longer follow up, and the conference paper from Ohlwein was replaced by the subsequent peer-reviewed publication (18).

Regarding incidence of diabetes, there was only one eligible cohort study for aircraft noise (24) and a second cohort for road traffic and railway noise exposure (23) at the time of the WHO review (6, 7). Since then, several more studies have been published and were included in the review by Zare Sakhividi (9). This was considered the start MA, to which only one entirely new study (13) was identified and incorporated here. Summary information for the retained studies for both IHD and diabetes incidence is shown in Annex 2.

In selecting the risk estimates for extraction the following decisions were taken according to the *a priori* defined criteria (see section 2.1). The diabetes study by Clark (25) used modelled community noise, identifying road traffic as the predominant transportation noise source. The risk estimate was thus included in the meta-analysis for diabetes and road traffic noise only. Both Clark (25) and Cai (12) presented several models adjusted for air pollution and according to the criteria the NO<sub>x</sub>-adjusted risk estimates were extracted.

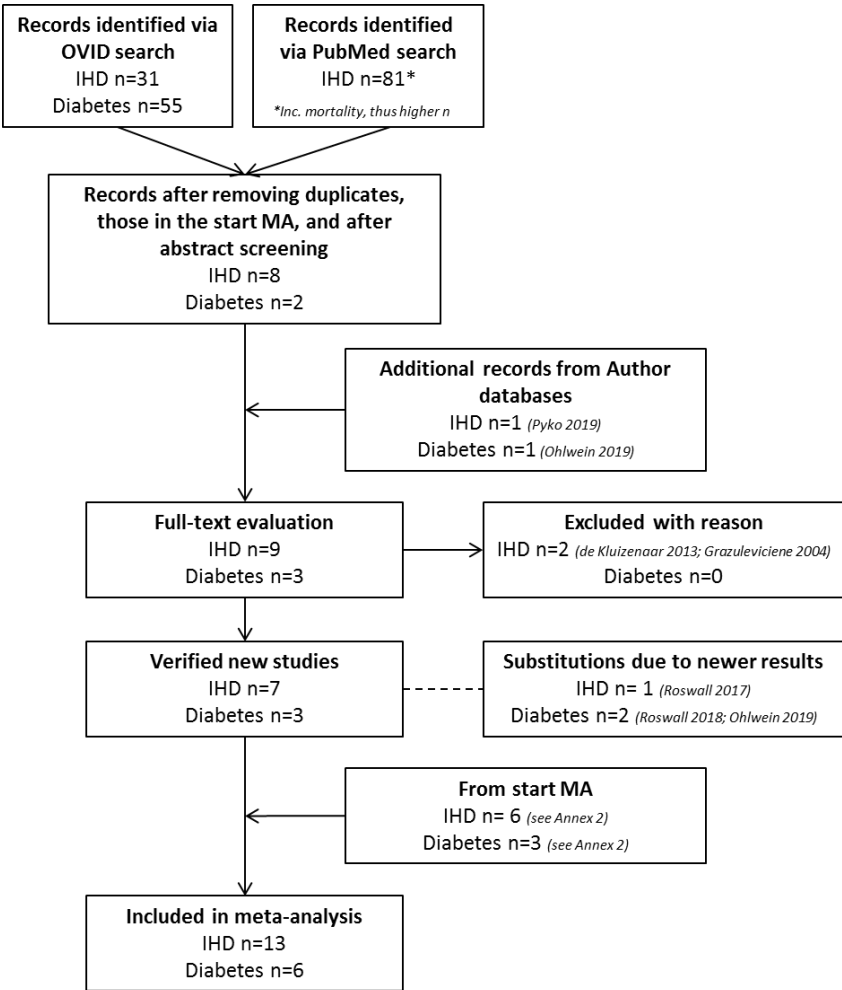


Figure 1 – Study selection

### 3.2 Meta-analysis and evaluation

In total, 13 studies were included in the IHD meta-analysis, by source contributing 13, 5 and 3 risk estimates respectively for road traffic (11-17, 26-29), aircraft (13, 15, 17, 30, 31) and railway (15-17) noise exposure.

As illustrated in Figure 2 and summarized in Table 1, the pooled RRs from these studies resulted in a respective 2%, 3% and 1% increased risk of IHD incidence per 10 dB increment in Lden. Only the result for road traffic noise reached statistical significance (1.02 [1.00 – 1.04] per 10 dB Lden). Further the studies on road traffic noise and IHD incidence showed negligible heterogeneity, and overall most studies were judged to have low risk of bias. The studies for aircraft noise were heterogeneous, and over half were judged to have high risk of bias. Though only a few studies were available, the heterogeneity amongst those included for railway noise was negligible and the studies were judged to have low risk of bias.

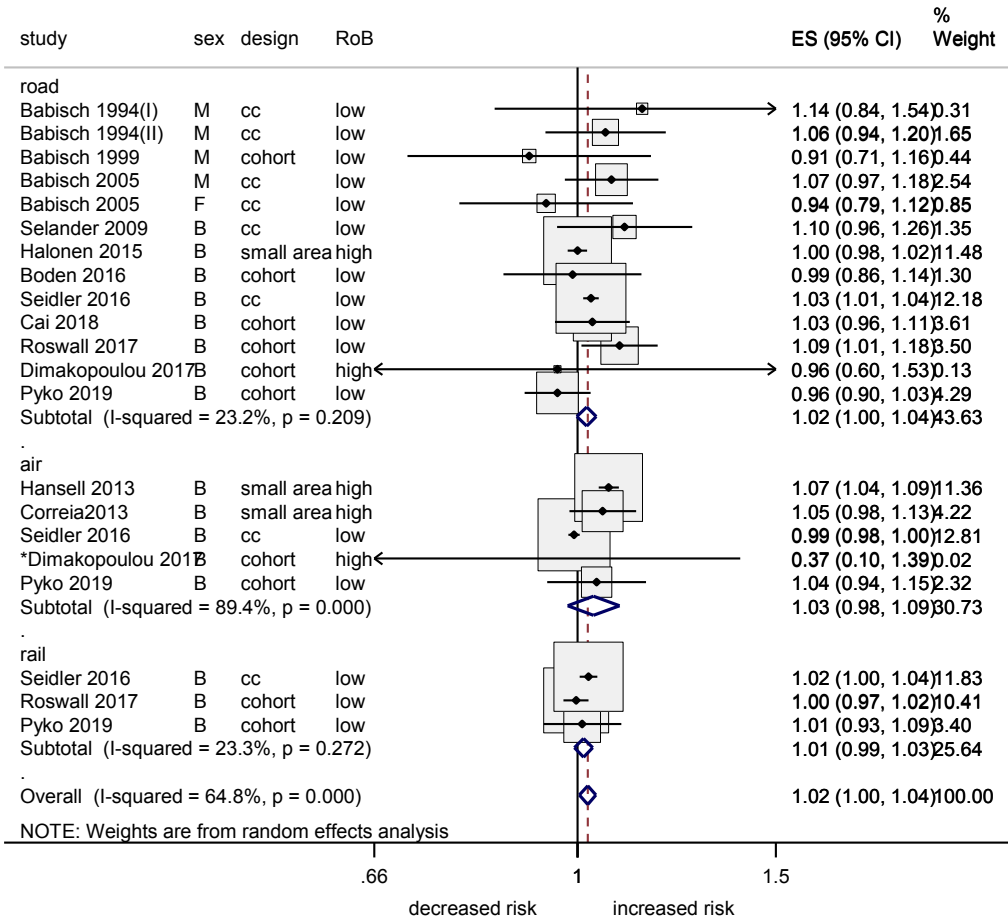


Figure 2 – Pooled association between IHD incidence and transportation noise (per 10 dB Lden) by source (\*Dimakopoulou indicates point estimate is off the scale)

For diabetes, a total of 6 studies were included, by source contributing 5, 3 and 2 risk estimates respectively for road traffic (1, 13, 18, 19, 25), aircraft (1, 13, 24) and railway (1, 19) noise exposure.

Figure 3 presents the pooled RRs by source, with the results also summarized in Table 1. For road traffic noise an 11% increased risk for diabetes incidence was found (1.11 [1.08 – 1.15] per 10 dB Lden). Heterogeneity amongst the 5 included cohort studies was negligible, and overall risk of bias for was determined to be low.

Full evaluation of the risk of bias is shown in Annex 3.

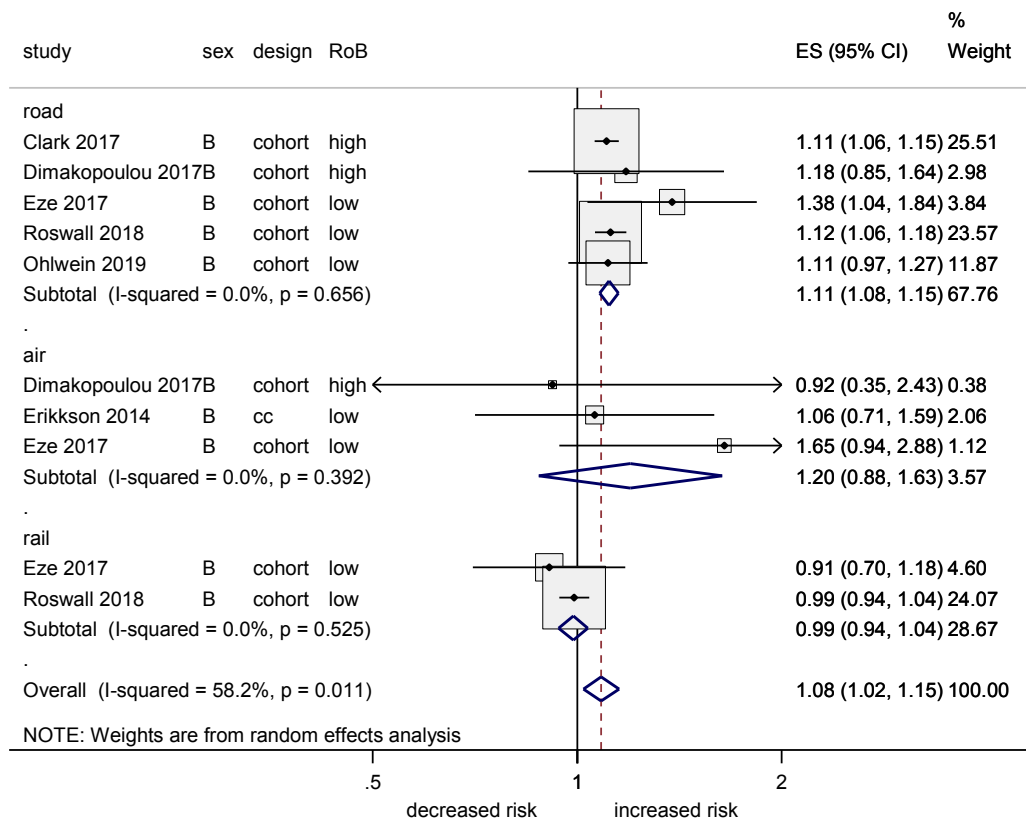


Figure 3 – Pooled association for diabetes incidence and transportation noise (per 10 dB Lden) by source

Table 1 – Summary of findings

Noise Source	No. Estimates by Study Design	RR per 10 dB Lden (95% CI)	Overall Risk of Bias <sup>a</sup>
IHD incidence			
Road traffic	6 cohort, 6 case-control, 1 small-area	1.02 (1.00 – 1.04)	Low (83%)
Aircraft	2 cohort, 1 case-control, 2 small-area	1.03 (0.98 – 1.09)	High (60%)
Railway	2 cohort, 1 case-control	1.01 (0.99 – 1.03)	Low (100%)
Diabetes incidence			
Road traffic	5 cohort	1.11 (1.08 – 1.15)	Low (60%)
Aircraft	2 cohort, 1 case-control	1.20 (0.88 – 1.63)	Low (66%)
Railway	2 cohort	0.99 (0.94 – 1.04)	Low (100%)

<sup>a</sup> Overall risk of bias designated as low or high if >50% of the studies for each noise source and outcome had low or high risk of bias, respectively.

#### 4. DISCUSSION

Since the cut-off date for inclusion of studies into the WHO guidelines, approximately 6 new studies each for both IHD and diabetes incidence have been published. This substantially adds to the growing body of evidence on the cardio-metabolic health effects of transportation noise. Further, most of the recent studies include several sources of transportation noise (1, 13, 15-17, 19), a trend that is

encouraging for strengthening the evidence to refine the exposure-response relationships, in particular for aircraft and railway noise exposure where studies were lacking in past. This trend also supports multi-pollutant modeling which can help distinguish the source, or combinations, driving the observed effects.

For IHD incidence the updated meta-analysis indicated a modest but statistically significant 2% increased risk per 10 dB Lden road traffic noise. The 3 and 1% respective risk increases for aircraft and railway noise were not statistically significant. While the point estimates are notably smaller than that reported in the WHO guidelines (i.e. 1.08 [1.01 – 1.15] per 10 dB Lden road traffic noise; 1.02 [1.00 – 1.15] per 10 dB Lden aircraft noise), the confidence intervals were also reduced, especially for road traffic noise. Two new large studies included for road traffic noise were influential in reducing the observed pooled effect with weights of over 30% (14, 17). Notably one was judged to have high risk of bias, thus additional large (preferably cohort studies often with lower risk of bias) in new study populations are justified.

Several of the IHD studies conducted categorical or non-parametric analyses to evaluate the form of the exposure-response functions. From these studies it could be concluded that the exposure-response function is approximately linear over the whole exposure range with lowest Lden levels typically around 35-45 dB. This implies that no threshold could be identified below which noise induced IHD risk can be excluded with a high level of certainty.

We did consider studies that exclusively considered IHD mortality. Of note, the results of the meta-analysis are in line with those for cardiovascular mortality from the SiRENE study (Short and Long Term Effects of Transportation Noise Exposure) (3) which included the entire adult population in Switzerland.

An insufficient number of studies on diabetes incidence and transportation noise were available for meta-analysis in the WHO guidelines. The new studies incorporated in Zare Sakhvidi (9) and here, however, suggest that transportation noise is an important risk factor for diabetes. Similar to IHD, most evidence relates to the association between road traffic noise with the updated exposure-response association showing a significant 11% increased risk (1.11 [1.08 – 1.15] per 10 dB Lden). Some of the included studies were judged to have high risk of bias. Also similar to IHD, the two most influential studies (weights over 30%) were not judged to have the same risk of bias (i.e. one was low, the other high). Again, approximately linear exposure-response functions were observed without any noticeable threshold above 35-45 dB.

## **5. CONCLUSIONS**

Consideration of the newest evidence on the cardio-metabolic health effects of transportation noise sources is paramount for setting appropriate regulatory limits to protect the population. This update of the WHO Environmental Noise Guidelines for the European Region showed that road traffic noise is an important risk factor for both IHD and diabetes incidence. Indications for an association for aircraft noise were also apparent, though the contributing studies were heterogeneous. The evidence for an association between railway noise and incidence of these cardio-metabolic diseases is at present less convincing, though this assessment is based on the small number of studies currently available.

## **ACKNOWLEDGEMENTS**

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## List of Annexes

### ANNEX 1: Search strings

- Ischemic Heart Disease (IHD)
  - OVID search – adapted from van Kempen (2018)
  - PubMed search – from Vienneau (2015)
- Diabetes
  - OVID Search – adapted from van Kempen (2018)

### ANNEX 2: Characteristics of the included studies

### ANNEX 3: Risk of Bias (RoB) assessment for included studies

- Risk of Bias tool (replicated and adapted from RIVM report pg. 53-54 (8))
- RoB evaluation: IHD studies
- RoB evaluation: Diabetes studies